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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/526,193	03/15/00	HAYDEN M	50110/002005

HM22/0619

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EXAMINER	
STEADMAN, D	

ART UNIT	PAPER NUMBER
1652	4

DATE MAILED: 06/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/526,193	Applicant(s) HAYDEN ET AL.	
	Examiner David J. Steadman	Art Unit 1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *87-111* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *87-111* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 March 2000* is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5 and 6* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

Status of the Application

Claims 87-111 are pending.

Replacement of claims 1-86 with claims 87-111 in Paper No. 4, filed 11/17/00 is acknowledged.

In view of the language used in Paper No. 4 requesting to replace claims 1-86 with claims 87-111, the Examiner has affirmed cancellation of claims 1-86 in a telephone conversation with Paul Clark on 06/13/01.

Drawings

1. The drawings submitted with this application have not been reviewed by a draftsperson at this time. When formal drawings are submitted, the draftsperson will perform a review. Direct any inquiries concerning drawing review to the Drawing Review Branch (703) 305-8404.

2. The drawings are objected to by the Examiner because Figure 12 is partially unreadable due to holes punched through the text. The figures must include a top margin of at least 2.0 cm. (3/4 inch). Correction is required.

Specification/Informalities

3. The attempt to incorporate subject matter into this application by reference to a hyperlink embedded in the specification (for example, page 51, line 10) is improper. Incorporation of subject matter into the patent application by reference to a hyperlink and/or other forms of browser-executable code is considered to be an improper incorporation by reference. See MPEP

608.01 regarding hyperlinks in the specification and 608.01(p), paragraph I regarding incorporation by reference. All hyperlinks embedded in the specification should be removed.

4. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed, for example, "Methods of Isolating Modulators of Human ABC1".

5. Figures 3A-3E are listed in the "Brief Description of the Drawings" section. However, only a single figure 3 is present.

Claim Objections

6. Claims 87-99, 102, 104, 106, 107, 109, and 111 are objected to because of the recitation of "ABC1" and "WHAM". Abbreviations, unless otherwise obvious, should not be recited in the claims without at least once reciting the entire phrase, i.e., "ATP binding cassette transporter 1" or "Wisconsin Hypo-Alpha Mutant" for which the abbreviations are used. It is noted that Applicants have provided support for these abbreviations at pages 25 and 73, respectively. Appropriate corrections are required.

7. Claims 87, 88, 96, and 97 are objected to because of the following informalities: the term "whether candidate compound" is grammatically incorrect and should be replaced with, for example, "whether a candidate compound". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 87, 88, 90-94, and 96-111 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

9. The term "constituent of an HDL particle" in claim 88 (claims 100-108 and 111 dependent thereon) is unclear and confusing. The term "constituent of an HDL particle" is not defined by the claim nor the specification and the meaning of this term is unclear. It is suggested that the language "constituent of an HDL particle" be replaced with a term that has a more clearly identifiable meaning.

10. Claims 87 (claims 100-108 and 111 dependent thereon), 88 (claims 100-108 and 111 dependent thereon), 95 (claims 102, 104-108, and 111 dependent thereon), and 96 (claims 102 and 104-108, dependent thereon) are confusing because it is unclear whether the result of the recited methods is a determination of whether the compound modulates the biological activity of the ABC1 polypeptide. Because an ABC1 polypeptide inherently binds certain lipids, mere binding of the ABC1 polypeptide to the lipid is not a clear indication that a candidate compound modulates the biological activity of the ABC1 polypeptide. It is suggested that, for example, Applicants provide a statement regarding a change in a specific biological activity of the ABC1 polypeptide in the presence of the compound that does not occur in the absence of the compound.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

11. Claims 87-91, 93-95, 97-103, and 105-111 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 87 (claims 100-103, 105-108, and 111 dependent thereon), 88 (claims 100-103, 105-108, and 111 dependent thereon), 89 (claims 100, 103, and 109-111 dependent thereon), 90 (claims 100, 101, 103, 109, and 110 dependent thereon), 91 (claims 93, 94, 102, 109, 110, and 111 dependent thereon), 95 (claim 102, 105-108, and 111 dependent thereon), 97 (claim 102, 105-108, and 111 dependent thereon), 98 (claims 100, 101, 103, 105-108, and 111 dependent thereon), 99 (claims 100, 101, 103, and 105-108, dependent thereon), are directed to methods of determining whether a candidate compound modulates ABC1 biological activity or methods for determining whether a candidate compound is useful in modulating HDL-cholesterol levels using an ABC1 polypeptide from any source. The specification teaches the structure of only a single representative species of such ABC1 polypeptides, i.e., a human ABC1 polypeptide. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of being an ABC1 polypeptide. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

12. Claims 87-111 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) a method for determining whether a candidate

compound modulates biological activity of human ABC1 (hABC1) by measuring hABC1 interaction in a cell or cell-free system with HDL-cholesterol or casein kinase in the presence and absence of a candidate compound, wherein an increased binding affinity of hABC1 for HDL-cholesterol or casein kinase in the presence of the compound relative to binding affinity without the compound indicates that said compound modulates hABC1 binding or 2) a method for determining whether a candidate compound is useful in modulating HDL-cholesterol levels in a cell or cell free system by measuring the levels or transport of HDL-cholesterol by hABC1 in the presence and absence of a candidate compound, wherein altered levels or transport of HDL-cholesterol in the presence of the compound relative to levels or transport without the compound indicates that said compound modulates HDL-cholesterol levels, does not reasonably provide enablement for 1) a method for determining whether a candidate compound modulates any biological activity of any ABC1 polypeptide by measuring any ABC1 polypeptide interaction in a cell or cell-free system with any lipid or casein kinase in the presence and absence of a candidate compound, wherein an increased binding or interaction of an ABC1 polypeptide with the lipid or casein kinase in the presence of the compound relative to binding affinity without the compound indicates that said compound modulates the ABC1 polypeptide biological activity or 2) a method for determining whether a candidate compound is useful in modulating HDL-cholesterol levels in a cell or cell free system by measuring the levels or transport of any constituent of an HDL particle or any lipid by any ABC1 polypeptide in the presence and absence of a candidate compound, wherein altered levels or transport of any constituent of an HDL particle or any lipid in the presence of the compound relative to levels or transport without the compound indicates that said compound modulates HDL-cholesterol levels.

Claims 87-111 are so broad as to encompass: 1) a method for determining whether a candidate compound modulates any biological activity using any ABC1 polypeptide with any lipid or casein kinase or 2) a method for determining whether a candidate compound is useful in modulating HDL-cholesterol levels using an HDL particle or any lipid by any ABC1 polypeptide. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extreme number of ABC1 polypeptides, biological activities thereof, and lipids. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. In the instant case, the disclosure is limited to: 1) a method for determining whether a candidate compound modulates hABC1 binding or interaction with HDL-cholesterol or casein kinase or 2) a method for determining whether a candidate compound is useful in modulating hABC1-regulated HDL-cholesterol levels.

The specification does not support the broad scope of the claims which encompass: 1) a method for determining whether a candidate compound modulates any biological activity of an ABC1 polypeptide using any ABC1 polypeptide with any lipid or casein kinase or 2) a method for determining whether a candidate compound is useful in modulating HDL-cholesterol levels using an HDL particle or any lipid by any ABC1 polypeptide, because the specification does not establish: A) the predictability of any ABC1 polypeptide binding to any lipid, as not all ABC1 polypeptides interact with any lipid; B) the predictability of any ABC1 polypeptide interacting

with casein kinase, as the prior art discloses few interactions of ABC1 with other polypeptides, particularly casein kinase and not all ABC1 polypeptides may interact with casein kinase; C) a rational and predictable scheme for determining whether a candidate compound modulates any biological activity of any ABC1 polypeptide; and D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including: 1) a method for determining whether a candidate compound modulates any biological activity of an ABC1 polypeptide using any ABC1 polypeptide with any lipid or casein kinase or 2) a method for determining whether a candidate compound is useful in modulating HDL-cholesterol levels using an HDL particle or any lipid by any ABC1 polypeptide. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

13. No claim is in condition for allowance.

14. Claims 87-111 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, first and second paragraphs, set forth in this Office action.

Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4242. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Steadman, whose telephone number is (703) 308-3934. The Examiner can normally be reached Monday-Friday from 7:30 am to 2:00 pm and from 3:30 pm to 5:30 pm. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy, can be reached at (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Art Unit receptionist whose telephone number is (703) 308-0196.

David J. Steadman

Rebecca Prouty

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PRIMARY EXAMINER
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